(4 points each). In each of the following there are two or more statements. One is true. Usually, it is taken directly from your textbook or from my lecture. In other cases, it might come from the scientific literature. Others have been modified so as to be untrue or misleading. Circle the letter next to the correct statement. In some cases, you might not know enough to be sure that statement is correct but you should be able to identify the others as bogus in some way.

1. b) Max homodimers are transcriptional repressors, and it is only when Myc and Max come together in a heterodimer that a transcriptional activator is formed.

2. a) Epigenetics is the study of heritable changes in gene expression that occur without a change in DNA sequence.

3. DNase I hypersensitivity sites are typically:
   b) cell type-specific and intergenic.

4. a) The maintenance methylase Dnmt1 exhibits predominantly hemimethylase activity.

5. a) Inhibitors of histone deacetylase activate the metallothionein I promoter.

6. a) The autoregulatory Sxl protein promotes the synthesis of more of itself through RNA splicing, resulting in a productive mRNA, thereby acting as a self-reinforcing on/off switch.

7. a) Nonsense mediated decay is a cellular mechanism of mRNA surveillance leading to degradation of mRNAs bearing premature stop codons.

8. a) Epigenetic imprints generally persist throughout the life of a mammal, but are erased during the passage of a gene through the germ line into the next generation.

9. b) Autozygosity is a term used to refer to homozygosity by descent from a common ancestor.

10. a) Alleles at separate loci that are associated with each other at a frequency significantly higher than expected by chance are said to be in linkage disequilibrium.

11. b) Dozens of genes that contribute to complex genetic traits have been identified in the last few years by whole genome association mapping and our understanding of "genetic architecture" underlying these traits is rapidly improving.

There was a problem with the numbering (there was no question 12 on the exam). We have kept the numbering the same for the key.

13. a) In forward genetics, one starts with the mutant phenotype.
Thx78is pedigree shows a family affected by an autosomal dominant genetic disease. Genotypes for three markers, A, B and C, are shown.

14. (9 points; three points per pair of markers) For each individual in the third generation (III-1, III-2, III-3, III-4, III-5 and III-6) indicate whether they are recombinant, nonrecombinant or indeterminate for each pair of markers in this pedigree (Fill in each of the 18 squares with yes, no or maybe).

<table>
<thead>
<tr>
<th>individual</th>
<th>A B recombinant</th>
<th>B C recombinant</th>
<th>A C recombinant</th>
</tr>
</thead>
<tbody>
<tr>
<td>III-1</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>III-2</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>III-3</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>III-4</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>III-5</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>III-6</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

We took off 1 point per incorrect answer (a maximum of 9 off; you could not get less than 0, of course).

15. (3 pt.) Considering only the data for marker locus A (i.e. ignoring B and C), what is the approximate lod score for linkage between A and the disease gene with θ = 0?  

2 recombinants (individuals III-3 and III-5) between A1 (the marker) and the disease observed, therefore, θ = 0 (meaning “assuming no recombination”) results in a lod of -∞.

16. (3 pt.) Considering only the data for marker locus B, what is the approximate lod score for linkage between B and the disease gene with θ = 0?  

There are no observed recombinants between B1 and the disease, therefore, the lod score is = .3n or 1.8
17. (3 pt.) Considering only the data for marker locus C, what is the approximate lod score for linkage between C and the disease gene with θ = 0?

1 recombinants (individual III-3) between C1 (the marker) and the disease observed, therefore, θ = 0 (meaning “assuming no recombination”) results in a lod of -∞.

18. (6 pt.) Other researchers in the field have reported that the disease gene is not present in an interval containing all three markers (A, B and C). Which of the following genetic maps is most likely, putting that information together with your pedigree (D stands for disease)?

c) ACBD – You observe 2 A-B recombinants in question 14, and only 1 A-C and 1 B-C recombinant, therefore A-B should be further apart than A-C and B-C. Thus, the order of the markers is ACB (or BCA). Since the disease is at a separate locus from the markers, looking at questions 15-17 allows you to identify that D is most closely tied to marker B (no recombinants between B and disease) so your answer is c) ACBD.

19. (6 pt.) Do you expect Sxl to be subject to nonsense-mediated decay in Drosophila males? Explain.

Yes. Sxl mRNA in males has a premature stop codon due to splicing without the aid of early expressed Sxl, therefore, this mRNA is then degraded via nonsense-mediated decay. You must mention the premature stop codon and splicing in your answer for full credit.

20. (6 pt.) How are the phenomena you defined on the next page related to each other? Do they tend to be true of the same traits? What kind of traits? Give a few examples. [You may want to answer the questions on the next page first. If you need more space, use the back of this page, but be sure to tell us.]

A variety of answers were accepted, but these phenomena usually affect the same traits, which are complex traits (the following phenomena are not complex traits in and of themselves, but usually characterize them). Common examples mentioned include cancer, heart disease, and cystic fibrosis.

Define the following terms (4 points each):

incomplete penetrance – not everyone with a genotype shows the associated phenotype

phenocopy – not everyone with the phenotype has the associated genotype

genetic heterogeneity – several different genotypes result in a single identical phenotype

polygenic determination – multiple loci influence the trait of interest